WHAT IS CLAIMED IS:

SUB B1

1. A system for recommending an optimal treatment protocol for an individual comprising:

a system model;

a plurality of treatment protocols;

a system model modifier, wherein said system model is modified by the system model modifier based on parameters specific to the individual; and

a selector to select an optimal treatment protocol from said plurality of treatment protocols based on the modified system model.

2. The system of claim 1 wherein the system model further comprises:

a realistic biological process model; and

a realistic treatment model that models the effects of a treatment on said biological process.

3. The system of claim 2, wherein said biological process model comprises mathematical models for biological processes affecting healthy cell populations and biological processes affecting cell populations with at least one disease.

4. The system of claim 3 wherein said healthy cell populations include bone-marrow cells and host tissue cells that are affected by said treatment model.

SUB A1

5. The system of claim 3 wherein said cell populations with at least one disease is

SUB A1 CONT.

one of cancer cells, and diseased bone-marrow cells including diseased Neutrophil cells and diseased Thrompocyte cells.

SUB B2

6. The system of claim 2, wherein said treatment models comprise treatment specific processes that affect cell populations.

7. The system of claim 6 wherein said treatment specific process is interactions involving one of a group comprising pharmacokinetic, pharmacodynamic, cytostatic, cytotoxic, and methods of affecting cell biology and causing cell death, with associated biological processes.

SUB A2

8. The method of claim 1 wherein, said parameters specific to the individual include one or more selected from a group consisting of parameters related to the biological process' dynamics, patient specific drug PK, PD and dynamics of dose-limiting host tissues.

9. The method of claim 8, wherein said parameters related to biological process' dynamics comprise age, weight, gender, blood picture, desired length of treatment protocol, previous reaction to treatment, molecular markers, genetic markers, pathologic specifics and cytologic specifics.

SUB B3

10. The system of claim 1, wherein the selector incorporates user-specific parameters in performing selection.

11. The system of claim 10 wherein said incorporation is done by using a fitness function.

12. The system of claim 11 wherein said fitness function incorporates at least one parameter selected from a group comprising patient survival, time to death, time to reach a specified disease stage (including cure), tumor load, pathogen load, cytotoxicity, side effects, quality of life, cost of treatment, and pain.

13. The system of claim 12, wherein a user can input specific coefficients for said at least one parameter to adjust the fitness function to satisfy the user's goals.

14. The system of claim 10, wherein the user-specific parameters are based on a user, said user being a medical doctor.

15. The system of claim 10, wherein the user-specific parameters are based on a user, said user being a scientist.

16. The system of claim 10, wherein the user-specific parameters are based on a user, said user being a drug developer.

SUB B6

17. The system of claim 1 wherein said selection of treatment protocols incorporate cytotoxic effects.

18. The system of claim 1 wherein said selection of treatment protocols incorporate drug efficacy.

19. The system of claim 1, wherein the selector performs the selection using operation research methods.

20. The system of claim 1, wherein the selector further comprises heuristics, said heuristics being used to perform searching and selection.

21. The system of claim 20 wherein, said heuristics comprise computational feasibility.

22. The system of claim 1 wherein said recommendation is a combination of disease and treatment strategy, including types of treatment, e.g. chemotherapy, radiotherapy, surgery, immunotherapy, etc, device, drug or drug combination and treatment schedule and dosage.

23. The system of claim 1, wherein, said system is implemented over a distributed computing system.

24. The system of claim 23, wherein the distributed computing system is the Internet.

25. The system of claim 23, wherein a user uses the system remotely.

26. A system for recommending an optimal treatment protocol for a general patient comprising:

a system model;

a plurality of treatment protocols; and

a selector to select an optimal treatment protocol from said plurality of treatment protocols based on the system model.

27. The system of claim 26 wherein the system model further comprises:

a realistic biological process model; and

a realistic treatment model that models the effects of a treatment on said biological process.

28. The system of claim 27, wherein said biological process model comprises mathematical models for biological processes affecting healthy cell populations and biological processes affecting cell populations with at least one disease.

29. The system of claim 28 wherein said healthy cell populations include bone-marrow cells and host tissue cells that are affected by said treatment model.

30. The system of claim 28 wherein said cell populations with at least one disease is one of cancer cells, and diseased bone-marrow cells including diseased Neutrophil cells and diseased Thrompocyte cells.

31. The system of claim 27, wherein said treatment models comprise treatment specific processes that affect cell populations.

32. The system of claim 31 wherein said treatment specific process is interactions involving one of a group comprising pharmacokinetic, pharmacodynamic, cytostatic, cytotoxic, and methods of affecting cell biology and causing cell death, with associated biological processes.

33. The system of claim 26, wherein the selector incorporates user-specific parameters in performing selection.

34. The system of claim 33 wherein said incorporation is done by using a fitness function.

35. The system of claim 34 wherein said fitness function incorporates at least one parameter selected from a group comprising patient survival, time to death, time to reach a specified disease stage (including cure), tumor load, pathogen load, cytotoxicity, side effects, quality of life, cost of treatment and pain.

36. The system of claim 35, wherein a user can input specific coefficients for said at least one parameter to adjust the fitness function to satisfy the user's goals.

37. The system of claim 33, wherein the user-specific parameters are based on a user,

said user being a medical doctor.

38. The system of claim 33, wherein the user-specific parameters are based on a user, said user being a scientist.

39. The system of claim 33, wherein the user-specific parameters are based on a user, said user being a drug developer.

40. The system of claim 26 wherein said selection of treatment protocols incorporate cytotoxic effects.

41. The system of claim 26 wherein said selection of treatment protocols incorporate drug efficacy.

42. The system of claim 26, wherein the selector performs the selection using operation research methods.

43. The system of claim 26, wherein the selector further comprises heuristics, said heuristics being used to perform searching and selection.

44. The system of claim 43 wherein, said heuristics comprise computational feasibility.

SUB B11

45. The system of claim 26 wherein said recommendation is a combination of disease and treatment strategy, including types of treatment, e.g. chemotherapy, radiotherapy, surgery, immunotherapy, etc, device, drug or drug combination and treatment schedule and dosage.

46. The system of claim 26, wherein, said system is implemented over a distributed computing system.

47. The system of claim 46, wherein the distributed computing system is the Internet.

SUB B12

48. The system of claim 46, wherein a user uses the system remotely.

49. The system of claim 48, wherein the remote system is a telephone.

SUB B13

50. A system for predicting progression of a biological process in an individual patient under a plurality of treatment protocols, wherein said biological process could be related to healthy or diseased processes, said plurality of protocols including no treatment, said system comprising:

a system model;

a plurality of treatment protocols; and

a system model modifier, wherein said system model is modified by the system model modifier based on parameters specific to the individual.

a predictor to predict the progression of at least one of the disease and the natural biological process under said plurality of treatment protocols based on the modified system

model.

51. The system of claim 50 wherein the system model further comprises:

a realistic biological process model; and

a realistic treatment model that models the effects of a treatment on said biological process.

52. The system of claim 51, wherein said biological process model comprises mathematical models for biological processes affecting healthy cell populations and biological processes affecting cell populations with at least one disease.

53. The system of claim 52 wherein said healthy cell populations include bone-marrow cells and host tissue cells that are affected by said treatment model.

54. The system of claim 52 wherein said cell populations with at least one disease is one of cancer cells, and diseased bone-marrow cells including diseased at least one of Neutrophil cells and diseased Thrombocyte cells.

55. The system of claim 51, wherein said treatment models comprise treatment specific processes that affect cell populations.

56. The system of claim 55 wherein said treatment specific process is interactions involving one of a group comprising PK, PD, drug cytostatics, drug cytotoxics, and methods of

affecting cell biology and causing cell death, with associated biological processes.

57. The system of claim 50 wherein, said parameters specific to the individual include one or more selected from a group consisting of parameters related to the biological process' dynamics, patient specific drug PK, PD and dynamics of dose-limiting host tissues.

58. The system of claim 57, wherein said parameters related to biological process' dynamics comprise age, weight, gender, blood picture, desired length of treatment protocol, previous reaction to treatment, molecular markers, genetic markers, pathologic specifics and cytologic specifics.

59. A system for predicting progression of a biological process in a general patient under a plurality of treatment protocols, wherein said biological process could be healthy or diseased processes, said plurality of protocols including no treatment, said system comprising:

a system model;

a plurality of treatment protocols; and

a predictor to predict the progression of the disease or the natural biological process under said plurality of treatment protocols.

60. The system of claim 59 wherein the system model further comprises:

a realistic biological process model; and

a realistic treatment model that models the effects of a treatment on said biological process.

61. The system of claim 60, wherein said biological process model comprises mathematical models for biological processes affecting healthy cell populations and biological processes affecting cell populations with at least one disease.

62. The system of claim 61 wherein said healthy cell populations include bone-marrow cells as well as other host tissue cells that are affected by said treatment model.

63. The system of claim 62 wherein said cell populations with at least one disease is one of cancer cells, and diseased bone-marrow cells including diseased Neutrophil cells and diseased Thrombocyte cells.

64. The system of claim 60, wherein said treatment models comprise treatment specific processes that affect cell populations.

65. The system of claim 64 wherein said treatment specific process is interactions involving one of a group comprising PK, PD cytostatic, cytotoxic, and methods of affecting cell biology and causing cell death, with associated biological processes.

66. A system for modelling Thrombopietic lineage in an individual, said system comprising:

a Thrombopoiesis system model including a realistic process progression model, for cells involved in Thrombopoiesis, said progression model including multiplication and

differentiation; and

a system model modifier, wherein said Thrombopoiesis system model is modified by the system model modifier based on parameters specific to the individual.

67. The system of claim 66 wherein the system model incorporates a realistic progression of cells involved in diseased Thrombopoiesis.

68. The system of claim 67 wherein diseased Thrombopoiesis includes Thrombocytopenia.

69. The system of claim 67 wherein the system model incorporates effects of at least one drug in the realistic progression of cells involved in Thrombopoiesis.

70. The system of claim 69 wherein said at least one drug is Thrombopoietin (TPO).

71. The system of claim 67 wherein said process model imitates a course of the individual's bone marrow progression, peripheral platelet counts and TPO concentration changes.

72. The system of claim 67, wherein said process model incorporates cell-suppressive treatment effects and administration of TPO to the patient.

73. The system of claim 72, wherein said cell-suppressive treatment can be chemotherapy.

74. The system of claim 66 wherein said process model further comprises a plurality of compartments.

75. The system of claim 74 wherein said compartments include:

a stem cell (SC) compartment that comprises bone marrow haemopoietic progenitors that have an ability to differentiate into more than one cell line wherein cells in the stem cell compartment proliferate and differentiate into one of megakaryocyte progenitors;

a colony forming units - megakaryocytes (CFU-Meg) compartment, wherein the megakaryocyte progenitors get committed as a megakaryocyte line and spend some time multiplying and maturing;

a megakaryoblast (MKB) compartment, which receives the cells from CFU-Meg, wherein the cells in the MKB compartment have lost their ability to proliferate but are not mature to release platelets;

a MK16 compartment, which receives cells from the MKB compartment, wherein a subset of cells in the MK16 compartment release platelets at a constant rate until they exhaust their capacity and are disintegrated and a second subset of cells do not release platelets but continue with endomitosis;

a MK32 compartment that receives cells from the MK16 compartment, wherein a subset of cells in this compartment release platelets and a second subset of cells do not release platelets but continue with endomitosis;

a MK64 compartment that receives cells from the MK32 compartment wherein a subset of cells in this compartment release platelets and a second subset of cells do not release platelets

20 but continue with endomitosis;

a MK128 compartment that receives cells from the MK64 compartment wherein a subset of cells in this compartment release platelets;

a platelets (PL) compartment.

76. The system of claim 75 wherein an effect of apoptosis is included with an overall effect of cell proliferation in giving rise to an amplification of cell numbers in a corresponding compartment.

77. The system of claim 75 wherein the process model further incorporates the effects of TPO on the SC, CFU-Meg and MKB compartments.

78. The system of claim 77 wherein the effects are expressed in terms of effects of TPO concentration on amplification rate, rate of cell maturation and a fraction of cells that undergo endomitosis.

79. The system of claim 78 wherein when the TPO concentration is above a predetermined threshold level, the amplification rate of cells in the SC compartment are affected and below the threshold the amplification rate is dependent only on a current number of cells.

80. The system of claim 77 wherein in the CFU-Meg compartment the cells are sensitive to TPO concentration regardless of the concentration of TPO.

81. The system of claim 77, wherein the transit time is same in all platelet releasing compartments and the transit time of the SC, CFU-Meg and MKB compartments are functions of micro-environmental conditions.

82. The system of claim 81 wherein in the SC compartment when the TPO concentration is above the threshold, the transit time is shortened based the dose.

83. The system of claim 81 wherein in the CFU-Meg and MKB, the transit time is solely based on TPO concentration.

84. The system of claim 77 wherein a fraction of cells in the SC compartment that commits to megakaryocytic lineage is constant.

85. The system of claim 77 wherein in the CFU-Meg and MKB compartments, every mature cell passes on to the next compartment.

86. The system of claim 77 wherein in the MK16, MK32 and MK64 compartments, a fraction of cells pass on to the next compartment, said fraction being dependent on the TPO concentration.

87. The system of claim 77 wherein cells from MK128 compartment do not flow into any other compartment.

88. The system of claim 74, wherein each of said compartments is further divided into sub-compartments, each of said sub-compartments containing cells of a specific age in hours.

89. The system of claim 88 wherein cells that spend all their corresponding transit time in a given compartment pass on to the next compartment, wherein cells that have left a corresponding compartment each hour fill the first sub-compartment of the next compartment.

90. The system of claim 88, wherein the platelet releasing cells contribute platelets to the first sub-compartment of the PL compartment.

91. The system of claim 66, wherein said model is used for recommending an optimal treatment protocol, wherein said system further comprises:

a plurality of treatment protocols; and

a selector to select an optimal treatment protocol from said plurality of treatment protocols based on the modified system model.

92. A system for modelling Thrombopietic lineage in a general patient, said system comprising a Thrombopoiesis system model including a realistic process model for cells involved in Thrombopoiesis.

93. The system of claim 92 wherein the system model incorporates a realistic progression of cells involved in diseased Thrombopoiesis.

94. The system of claim 93 wherein diseased Thrombopoiesis includes Thrombocytopenia.

95. The system of claim 93 wherein the system model incorporates effects of at least one drug in the realistic progression of cells involved in Thrombopoiesis.

96. The system of claim 95 wherein said at least one drug is Thrombopoietin (TPO).

97. The system of claim 93 wherein said process model imitates a course of the patient's bone marrow progression, peripheral platelet counts and TPO concentration changes.

98. The system of claim 93, wherein said process model incorporates cell-suppressive treatment effects and administration of TPO to the patient.

99. The system of claim 98, wherein said cell-suppressive treatment is chemotherapy.

100. The system of claim 92 wherein said process model further comprises a plurality of compartments.

101. The system of claim 100 wherein said compartments include:

a stem cell (SC) compartment that comprises bone marrow hemopoietic progenitors that have an ability to differentiate into more than one cell line wherein cells in the stem cell compartment proliferate and differentiate into one of megakaryocyte progenitors;

a colony forming units - megakaryocytes (CFU-Meg) compartment, wherein the megakaryocyte progenitors get committed as a megakaryocyte line and spend some time multiplying and maturing;

a megakaryoblast (MKB) compartment, which receives the cells from CFU-Meg, wherein the cells in the MKB compartment have lost their ability to proliferate but are not mature to release platelets;

a MK16 compartment, which receives cells from the MKB compartment, wherein a subset of cells in the MK16 compartment release platelets at a constant rate until they exhaust their capacity and are disintegrated and a second subset of cells do not release platelets but continue with endomitosis;

a MK32 compartment that receives cells from the MK16 compartment, wherein a subset of cells in this compartment release platelets and a second subset of cells do not release platelets but continue with endomitosis;

a MK64 compartment that receives cells from the MK32 compartment wherein a subset of cells in this compartment release platelets and a second subset of cells do not release platelets but continue with endomitosis;

a MK128 compartment that receives cells from the MK64 compartment wherein a subset of cells in this compartment release platelets;

a platelets (PL) compartment.

102. The system of claim 101 wherein an effect of apoptosis are included with an overall effect of cell proliferation in giving rise to an amplification of cell numbers in a corresponding compartment.

103. The system of claim 101 wherein the process model further incorporates the effects of TPO on the SC, CFU-Meg and MKB compartments.

104. The system of claim 103 wherein the effects are expressed in terms of effects of TPO concentration on amplification rate, rate of cell maturation and a fraction of cells that undergo endomitosis.

105. The system of claim 104 wherein when the TPO concentration is above a predetermined threshold level, the amplification rate of cells in the SC compartment are affected and below the threshold the amplification rate is dependent only on a current number of cells.

106. The system of claim 103 wherein in the CFU-Meg compartment the cells are sensitive to TPO concentration regardless of the concentration of TPO.

107. The system of claim 103, wherein the transit time is same in all platelet releasing compartments and the transit time of the SC, CFU-Meg and MKB compartments are functions of micro-environmental conditions.

108. The system of claim 107 wherein in the SC compartment when the TPO concentration is above the threshold, the transit time is shortened based the dose.

109. The system of claim 107 wherein in the CFU-Meg and MKB, the transit time is

solely based on TPO concentration.

110. The system of claim 103 wherein a fraction of cells in the SC compartment that commits to megakaryocytic lineage is constant.

111. The system of claim 103 wherein in the CFU-Meg and MKB compartments, every mature cell passes on to the next compartment.

112. The system of claim 103 wherein in the MK16, MK32 and MK64 compartments, a fraction of cells pass on to the next compartment, said fraction being dependent on the TPO concentration.

113. The system of claim 103 wherein cells from MK128 compartment do not flow into any other compartment.

114. The system of claim 100, wherein each of said compartments is further divided into sub-compartments, each of said sub-compartments containing cells of a specific age in hours.

115. The system of claim 114 wherein cells that spend all their corresponding transit time in a given compartment pass on to the next compartment, wherein cells that have left a corresponding compartment each hour fill the first sub-compartment of the next compartment.

116. The system of claim 115, wherein the platelet releasing cells contribute platelets to the first sub-compartment of the PL compartment.

117. The system of claim 92, wherein said model is used for recommending an optimal treatment protocol, wherein said system further comprises:

a plurality of treatment protocols; and

a selector to select an optimal treatment protocol from said plurality of treatment protocols based on the modified system model.

118. A system for predicting progression of Thrombopoiesis and a model of Thrombocytopenia for an individual under a plurality of treatment protocols, said plurality of protocols including no treatment, said system comprising:

a Thrombopoiesis and a Thrombocytopenia system model;

a plurality of treatment protocols for affecting Thrombopoiesis and treating Thrombocytopenia using at least one drug;

a system model modifier, wherein saidThrombopoiesis and Thrombocytopenia system models are modified by the system model modifier based on parameters specific to the individual; and

a predictor to predict the progression of the disease or the natural biological process under said plurality of treatment protocols based on the modified system model.

119. The system of claim 118 wherein the system model incorporates a realistic progression of cells involved in diseased Thrombopoisis.

120. The system of claim 119 wherein diseased Thrombopoiesis includes Thrombocytopenia.

121. The system of claim 119 wherein the system model incorporates effects of at least one drug on the realistic progression of cells involved in Thrombocytopenia.

122. The system of claim 121 wherein said at least one drug is Thrombopoietin (TPO).

123. The system of claim 119 wherein said process model imitates a course of the individual's bone marrow progression, peripheral platelet counts and TPO concentration changes.

124. The system of claim 119, wherein said process model incorporates cell-suppressive treatment effects and administration of TPO to the patient.

125. The system of claim 124, wherein said cell-suppressive treatment is chemotherapy.

126. The system of claim 118 wherein said process model further comprises a plurality of compartments.

127. The system of claim 126 wherein said compartments include:

a stem cell (SC) compartment that comprises bone marrow hemopoietic progenitors that have an ability to differentiate into more than one cell line wherein cells in the stem cell compartment proliferate and differentiate into one of megakaryocyte progenitors;

a colony forming units - megakaryocytes (CFU-Meg) compartment, wherein the megakaryocyte progenitors get committed as a megakaryocyte line and spend some time multiplying and maturing;

a megakaryoblast (MKB) compartment, which receives the cells from CFU-Meg, wherein the cells in the MKB compartment have lost their ability to proliferate but are not mature to release platelets;

a MK16 compartment, which receives cells from the MKB compartment, wherein a subset of cells in the MK16 compartment release platelets at a constant rate until they exhaust their capacity and are disintegrated and a second subset of cells do not release platelets but continue with endomitosis;

a MK32 compartment that receives cells from the MK16 compartment, wherein a subset of cells in this compartment release platelets and a second subset of cells do not release platelets but continue with endomitosis;

a MK64 compartment that receives cells from the MK32 compartment wherein a subset of cells in this compartment release platelets and a second subset of cells do not release platelets but continue with endomitosis;

a MK128 compartment that receives cells from the MK64 compartment wherein a subset of cells in this compartment release platelets;

a platelets (PL) compartment.

128. The system of claim 127 wherein an effect of apoptosis are included with an overall effect of cell proliferation in giving rise to an amplification of cell numbers in a corresponding compartment.

129. The system of claim 127 wherein the process model further incorporates the effects of TPO on the SC, CFU-Meg and MKB compartments.

130. The system of claim 129 wherein the effects are expressed in terms of effects of TPO concentration on amplification rate, rate of cell maturation and a fraction of cells that undergo endomotisis.

131. The system of claim 130 wherein when the TPO concentration is above a predetermined threshold level, the amplification rate of cells in the SC compartment are affected and below the threshold the amplification rate is dependent only on a current number of cells.

132. The system of claim 129 wherein in the CFU-Meg compartment the cells are sensitive to TPO concentration regardless of the concentration of TPO.

133. The system of claim 129, wherein the transit time is same in all platelet releasing compartments and the transit time of the SC, CFU-Meg and MKB compartments are functions of micro-environmental conditions.

134. The system of claim 133 wherein in the SC compartment when the TPO concentration is above the threshold, the transit time is shortened based the dose.

135. The system of claim 133 wherein in the CFU-Meg and MKB, the transit time is solely based on TPO concentration.

136. The system of claim 135 wherein a fraction of cells in the SC compartment that commits to megakaryocytic lineage is constant.

137. The system of claim 129 wherein in the CFU-Meg and MKB compartments, every mature cell passes on to the next compartment.

138. The system of claim 129 wherein in the MK16, MK32 and MK64 compartments, a fraction of cells pass on to the next compartment, said fraction being dependent on the TPO concentration.

139. The system of claim 129 wherein cells from MK128 compartment do not flow into any other compartment.

140. The system of claim 126, wherein each of said compartments is further divided into sub-compartments, each of said sub-compartments containing cells of a specific age in hours.

141. The system of claim 140 wherein cells that spend all their corresponding transit time in a given compartment pass on to the next compartment, wherein cells that have left a corresponding compartment each hour fill the first sub-compartment of the next compartment.

142. The system of claim 141, wherein the platelet releasing cells contribute platelets to the first sub-compartment of the PL compartment.

143. A system for predicting progression of Thrombopoiesis and a model of Thrombocytopenia for a general patient under a plurality of treatment protocols, said plurality of protocols including no treatment, said system comprising:

a Thrombopoiesis and a Thrombocytopenia system model;

a plurality of treatment protocols for affecting Thrombopoiesis and treating Thrombocytopenia using at least one drug; and

a predictor to predict the progression of the disease or the natural biological process under said plurality of treatment protocols based on the modified system model.

144. The system of claim 143 wherein the system model incorporates a realistic progression of cells involved in diseased Thrombopoiesis

145. The system of claim 144 wherein diseased Thrombopoiesis includes Thrombocytopenia.

146. The system of claim 144 wherein the system model incorporates effects of at least

one drug in the realistic progression of cells involved in Thrombocytopenia

147. The system of claim 146 wherein said at least one drug is Thrombopoietin (TPO).

148. The system of claim 144 wherein said process model imitates a course of the individual's bone marrow progression, peripheral platelet counts and TPO concentration changes.

149. The system of claim 144, wherein said process model incorporates cell-suppressive treatment effects and administration of TPO to the patient.

150. The system of claim 149, wherein said cell-suppressive treatment is chemotherapy.

151. The system of claim 144 wherein said process model further comprises a plurality of compartments.

152. The system of claim 151 wherein said compartments include:

a stem cell (SC) compartment that comprises bone marrow hemopoietic progenitors that have an ability to differentiate into more than one cell line wherein cells in the stem cell compartment proliferate and differentiate into one of megakaryocyte progenitors;

a colony forming units - megakaryocytes (CFU-Meg) compartment, wherein the megakaryocyte progenitors get committed as a megakaryocyte line and spend some time

multiplying and maturing;

a megakaryoblast (MKB) compartment, which receives the cells from CFU-Meg, wherein the cells in the MKB compartment have lost their ability to proliferate but are not mature to release platelets;

a MK16 compartment, which receives cells from the MKB compartment, wherein a subset of cells in the MK16 compartment release platelets at a constant rate until they exhaust their capacity and are disintegrated and a second subset of cells do not release platelets but continue with endomitosis;

a MK32 compartment that receives cells from the MK16 compartment, wherein a subset of cells in this compartment release platelets and a second subset of cells do not release platelets but continue with endomitosis;

a MK64 compartment that receives cells from the MK32 compartment wherein a subset of cells in this compartment release platelets and a second subset of cells do not release platelets but continue with endomitosis;

a MK128 compartment that receives cells from the MK64 compartment wherein a subset of cells in this compartment release platelets;

a platelets (PL) compartment.

153. The system of claim 152 wherein an effect of apoptosis are included with an overall effect of cell proliferation in giving rise to an amplification of cell numbers in a corresponding compartment.

154. The system of claim 152 wherein the process model further incorporates the

effects of TPO on the SC, CFU-Meg and MKB compartments.

155. The system of claim 154 wherein the effects are expressed in terms of effects of TPO concentration on amplification rate, rate of cell maturation and a fraction of cells that undergo endomotisis.

156. The system of claim 155 wherein when the TPO concentration is above a predetermined threshold level, the amplification rate of cells in the SC compartment are affected and below the threshold the amplification rate is dependent only on a current number of cells.

157. The system of claim 154 wherein in the CFU-Meg compartment the cells are sensitive to TPO concentration regardless of the concentration of TPO.

158. The system of claim 154, wherein the transit time is same in all platelet releasing compartments and the transit time of the SC, CFU-Meg and MKB compartments are functions of micro-environmental conditions.

159. The system of claim 158 wherein in the SC compartment when the TPO concentration is above the threshold, the transit time is shortened based the dose.

160. The system of claim 158 wherein in the CFU-Meg and MKB, the transit time is solely based on TPO concentration.

161. The system of claim 154 wherein a fraction of cells in the SC compartment that commits to megakaryocytic lineage is constant.

162. The system of claim 154 wherein in the CFU-Meg and MKB compartments, every mature cell passes on to the next compartment.

163. The system of claim 154 wherein in the MK16, MK32 and MK64 compartments, a fraction of cells pass on to the next compartment, said fraction being dependent on the TPO concentration.

164. The system of claim 154 wherein cells from MK128 compartment do not flow into any other compartment.

165. The system of claim 151, wherein each of said compartments is further divided into sub-compartments, each of said sub-compartments containing cells of a specific age in hours.

166. The system of claim 165 wherein cells that spend all their corresponding transit time in a given compartment pass on to the next compartment, wherein cells that have left a corresponding compartment each hour fill the first sub-compartment of the next compartment.

167. The system of claim 166, wherein the platelet releasing cells contribute platelets to the first sub-compartment of the PL compartment.

168. A system for modelling Neutrophil lineage for an individual, said system comprising:

a Neutrophil system model including a realistic process model for cells involved in Granulopoiesis; and

a system model modifier, wherein said Neutrophil system model is modified by the system model modifier based on parameters specific to the individual.

169. The system of claim 168 wherein the system model incorporates a realistic progression of cells involved in Granulopoietic disorders, including Neutropenia.

170. The system of claim 169 wherein the system incorporates effects of at least one drug in the realistic progression of cells involved in Granulopoiesis and Neutropenia.

171. The system of claim 170 wherein said at least one drug is Granulocyte Colony Stimulating Factor (G-CSF).

172. The system of claim 171 wherein said model comprises at least three stages,

a first stage related to an administered amount of cytokine;

a second stage representing a pharmacokinetic behavior of G-CSF; and

a third stage representing a phrmacodynamic effect of G-CSF on kinetic parameters of the system.

173. The system of claim 168 wherein said model comprises a mitotic compartment, and a post mitotic compartment, said mitotic compartment being divided into subcompartments wherein a kth sub-compartment contains cells of age between k-1 and k hours relative to a time of entry into the mitotic compartment.

174. The system of claim 173, wherein effects of toxic drugs, including chemotherapy are incorporated by mapping various cell-cycle phases to the sub-compartments and formulating a function of cytotoxic effects of toxic drugs, including chemotherapy on the cell-cycle phases.

175. The system of claim 173 wherein the effects of G-CSF on the mitotic compartment are modeled as an increase in a rate of cells entering the myeloblasts compartment from an uncommitted stem cell pool.

176. The system of claim 173 wherein the post-mitotic compartment is modeled as a single pool of cells wherein cells in a last sub-compartment of the mitotic compartment enters the post-mitotic compartment and a proportion of cells within the post-mitotic compartment enters a Neutrophil pool every hour.

177. The system of claim 173 wherein effects of G-CSF on the Neutrophil lineage are modeled as a decrease in the cells in the post-mitotic compartment which is subsequently compensated by an increased production in the mitotic compartment, said compensation sustaining an increase in mature Neutrophil count.

178. The system of claim 173, wherein an elimination of Neutrophils in the post-mitotic compartment is represented by a Poisson distribution.

179. The system of claim 173, wherein the cytotoxic effects of toxic drugs, including chemotherapy in the post-mitotic compartment is modeled as an effect on a single pool of cells.

180. The system of claim 173, wherein kinetic of G-CSF is modeled as an exponential distribution.

181. The system of claim 169, wherein a selection of an optimal treatment uses an objective function that aims at minimizing G-CSF administration and returning Neutrophil lineage to normal levels.

182. The system of claim 181, wherein said selection is performed using linear programming.

183. The system of claim 182, wherein phrmacokinetics and pharmacodynamics of G-CSF are defined using piecewise linear functions.

184. The system of claim 168, wherein said model is used for recommending an optimal treatment protocol, wherein said system further comprises:

a plurality of treatment protocols; and

a selector to select an optimal treatment protocol from said plurality of treatment protocols based

on the modified system model.

185. A system for modelling Neutrophil lineage for a general patient, said system comprising a Granulopoiesis system model including a realistic process model for cells involved in Neutrophil production.

186. The system of claim 185 wherein the system model incorporates a realistic progression of cells involved in Granulopoiesis disorders including Neutropenia.

187. The system of claim 186 wherein the system incorporates effects of at least one drug in the realistic progression of cells involved in Granulopoiesis disorders including Neutropenia.

188. The system of claim 187 wherein said at least one drug is Granulocyte Colony Stimulating Factor (G-CSF).

189. The system of claim 188 wherein said model comprises at least three stages,

a first stage related to an administered amount of cytokine;

a second stage representing a pharmacokinetic behavior of G-CSF; and

a third stage representing a phrmacodynamic effect of G-CSF on kinetic parameters.

190. The system of claim 185 wherein said model comprises a mitotic compartment, and a post mitotic compartment, said mitotic compartment being divided into subcompartments

wherein a kth sub-compartment contains cells of age between k-1 and k hours relative to a time of entry into the mitotic compartment.

191. The system of claim 190, wherein effects of toxic drugs, including chemotherapy are incorporated by mapping various cell-cycle phases to the sub-compartments and formulating a function of cytotoxic effects of toxic drugs, including chemotherapy on the cell-cycle phases.

192. The system of claim 190 wherein the effects of G-CSF on the mitotic compartment are modeled as an increase in a rate of cells entering the myeloblasts compartment from an uncommitted stem cell pool.

193. The system of claim 190 wherein the post-mitotic compartment is modeled as a single pool of cells wherein cells in a last sub-compartment of the mitotic compartment enters the post-mitotic compartment and a proportion of cells within the post-mitotic compartment enters a Neutrophil pool every hour.

194. The system of claim 190 wherein effects of G-CSF on the Neutrophil lineage are modeled as a decrease in the cells in the post-mitotic compartment which is subsequently compensated by an increased production in the mitotic compartment, said compensation sustaining an increase in Neutrophil count.

195. The system of claim 190, wherein an elimination of Neutrophils in the post-mitotic compartment is represented by a Poisson distribution.

196. The system of claim 190, wherein the cytotoxic effects of toxic drugs, including chemotherapy in the post-mitotic compartment is modeled as an effect on a single pool of cells.

197. The system of claim 190, wherein kinetic of G-CSF is modeled as an exponential distribution.

198. The system of claim 186, wherein a selection of an optimal treatment uses an objective function that aims at minimizing G-CSF administration and returning Neutrophil lineage to normal levels.

199. The system of claim 198, wherein said selection is performed using linear programming.

200. The system of claim 199, wherein phrmacokinetics and pharmacodynamics of G-CSF are defined using piecewise linear functions.

201. The system of claim 185, wherein said model is used for recommending an optimal treatment protocol, wherein said system further comprises:

a plurality of treatment protocols; and

a selector to select an optimal treatment protocol from said plurality of treatment protocols based on the modified system model.

202. A system for predicting progression of Granulopoiesis for an individual under a plurality of treatment protocols, said plurality of protocols including no treatment, said system comprising:

a Granulopoiesis system model including a realistic process model for cells involved in Neutrophil production;

a plurality of treatment protocols; and

a system model modifier, wherein said Neutrophil production system model is modified by the system model modifier based on parameters specific to the individual; and

a predictor that predicts the progression under the plurality of treatment protocols based on the modified system model.

203. The system of claim 202 wherein the system model incorporates a realistic progression of cells involved in Granulopoietic disorders, including Neutropenia.

204. The system of claim 203 wherein the system incorporates effects of at least one drug in the realistic progression of cells involved in Granulopoiesis and Neutropenia.

205. The system of claim 204 wherein said at least one drug is Granulocyte Colony Stimulating Factor (G-CSF).

206. The system of claim 205 wherein said model comprises at least three stages,

a first stage related to an administered amount of cytokine;

a second stage representing a pharmacokinetic behavior of G-CSF; and

a third stage representing a phrmacodynamic effect of G-CSF on kinetic parameters.

207. The system of claim 202 wherein said model comprises a mitotic compartment, and a post mitotic compartment, said mitotic compartment being divided into subcompartments wherein a kth sub-compartment contains cells of age between k-1 and k hours relative to a time of entry into the mitotic compartment.

208. The system of claim 207, wherein effects of toxic drugs, including chemotherapy are incorporated by mapping various cell-cycle phases to the sub-compartments and formulating a function of cytotoxic effects of toxic drugs, including chemotherapy on the cell-cycle phases.

209. The system of claim 207 wherein the effects of G-CSF on the mitotic compartment are modeled as an increase in a rate of cells entering the myeloblasts compartment from an uncommitted stem cell pool.

210. The system of claim 207 wherein the post-mitotic compartment is modeled as a single pool of cells wherein cells in a last sub-compartment of the mitotic compartment enters the post-mitotic compartment and a proportion of cells within the post-mitotic compartment enters a Neutrophil pool every hour.

211. The system of claim 207 wherein effects of G-CSF on the Neutrophil lineage are modeled as a decrease in the cells in the post-mitotic compartment which is subsequently compensated by an increased production in the mitotic compartment, said compensation

sustaining an increase in mature Neutrophil count.

212. The system of claim 207, wherein an elimination of Neutrophils in the post-mitotic compartment is represented by a Poisson distribution.

213. The system of claim 207, wherein the cytotoxic effects of toxic drugs, including chemotherapy in the post-mitotic compartment is modeled as an effect on a single pool of cells.

214. The system of claim 207, wherein kinetic of G-CSF is modeled as an exponential distribution.

215. The system of claim 203, wherein a selection of an optimal treatment uses an objective function that aims at minimizing G-CSF administration and returning Neutrophil lineage to normal levels.

216. The system of claim 215, wherein said selection is performed using linear programming.

217. The system of claim 216, wherein phrmacokinetics and pharmacodynamics of G-CSF are defined using piecewise linear functions.

218. A system for predicting progression of Granulopoiesis for a general patient under a plurality of treatment protocols, said plurality of protocols including no treatment, said system

comprising:

a Neutrophil system model including a realistic process model for cells involved in Neutrophil production;

a plurality of treatment protocols; and

a predictor that predicts the progression under the plurality of treatment protocols based on the modified system model.

219. The system of claim 218 wherein the system model incorporates a realistic progression of cells involved in Granulopoietic disorders, including Neutropenia.

220. The system of claim 219 wherein the system incorporates effects of at least one drug in the realistic progression of cells involved in Granulopoiesis and Neutropenia.

221. The system of claim 220 wherein said at least one drug is Granulocyte Colony Stimulating Factor (G-CSF).

222. The system of claim 221 wherein said model comprises at least three stages,

a first stage related to an administered amount of cytokine;

a second stage representing a pharmacokinetic behavior of G-CSF; and

a third stage representing a phrmacodynamic effect of G-CSF on kinetic parameters.

223. The system of claim 218 wherein said model comprises a mitotic compartment, and a post mitotic compartment, said mitotic compartment being divided into subcompartments wherein a kth sub-compartment contains cells of age between k-1 and k hours relative to a time

of entry into the mitotic compartment.

224. The system of claim 223, wherein effects of toxic drugs, including chemotherapy are incorporated by mapping various cell-cycle phases to the sub-compartments and formulating a function of cytotoxic effects of toxic drugs, including chemotherapy on the cell-cycle phases.

225. The system of claim 223 wherein the effects of G-CSF on the mitotic compartment are modeled as an increase in a rate of cells entering the myeloblasts compartment from an uncommitted stem cell pool.

226. The system of claim 223 wherein the post-mitotic compartment is modeled as a single pool of cells wherein cells in a last sub-compartment of the mitotic compartment enters the post-mitotic compartment and a proportion of cells within the post-mitotic compartment enters a Neutrophil pool every hour.

227. The system of claim 223 wherein effects of G-CSF on the Neutrophil lineage are modeled as a decrease in the cells in the post-mitotic compartment which is subsequently compensated by an increased production in the mitotic compartment, said compensation sustaining an increase in mature Neutrophil count.

228. The system of claim 223, wherein an elimination of Neutrophils in the post-mitotic compartment is represented by a Poisson distribution.

229. The system of claim 223, wherein the cytotoxic effects of toxic drugs, including chemotherapy in the post-mitotic compartment is modeled as an effect on a single pool of cells.

230. The system of claim 223, wherein kinetic of G-CSF is modeled as an exponential distribution.

231. The system of claim 219, wherein a selection of an optimal treatment uses an objective function that aims at minimizing G-CSF administration and returning Neutrophil lineage to normal levels.

232. The system of claim 231, wherein said selection is performed using linear programming.

233. The system of claim 232, wherein phrmacokinetics and pharmacodynamics of G-CSF are defined using piecewise linear functions.

234. A system for recommending an optimal treatment protocol for treating cancer using drugs, including chemotherapy, for an individual, said system comprising:

a cancer system model;

a plurality of treatment protocols for treating cancer using chemotherapy;

a system model modifier, wherein said cancer system model is modified by the system model modifier based on parameters specific to the individual; and

a selector to select an optimal treatment protocol from said plurality of treatment

protocols based on the modified system model.

235. The system of claim 234 wherein the system model further comprises:

a realistic process model of cancer development; and

a realistic treatment model that models the effects of treating cancer with drugs, including chemotherapy.

236. The system of claim 235 wherein said process model incorporates a distribution of cycling cells and quiescent cells.

237. The system of claim 235 where a tumor cell cycle is divided into at least four compartments G1, S, G2 and M and a quiescent stage is denoted by G0, wherein each of said four compartments is further subdivided into sub-compartments and an ith sub-compartment representing cells of age I in the corresponding compartment, wherein cells entering a compartment always enter a first sub-compartment of the compartment.

238. The system of claim 237 wherein the model traces development of cancer cells using a predetermined set of parameters by calculating a number of cells in each subcompartment using stepwise equations.

239. The system of claim 238 wherein a probability vector is used to determine a fraction of cells that leaves any subcompartment in a compartment to move to a first subcompartment of the next compartment.

240. The system of claim 238 where a set control functions uniquely determine an outcome of every single step, wherein said control functions depend on age of cells, state of a current population and associated environment.

241. The system of claim 238 wherein a tumor is modelled as a combination of a plurality of homogeneous group of cells, each of said homogeneous group of cells representing a similarly behaving group of cells distributed between all the cell-cycle compartments.

242. The system of claim 241, wherein in each step, a number of cells in each sub-compartment of each compartment of each group is calculated according to factors including a previous state, parameters of tumor, tumor current microenvironment and drug concentration.

243. The system of claim 242 where spatial structure of the tumor is included in the model.

SUB B19

244. The system of claim 243, wherein PK and PD, cytostatic effects, cytotoxic effects, and other effects on cell disintegration of anticancer drugs are incorporated into the model.

245. The system of claim 244 wherein a dose-limiting toxicity is incorporated into the model.

SUB A2

246. The system of claim 231 wherein, said parameters specific to the individual

SUB A3 CONT.

comprise parameters related to tumor dynamics, patient specific drug PK, and dynamics of dose-limiting host tissues.

247. The system of claim 246, wherein said parameters related to tumor dynamics comprise age, weight, gender, percentage of limiting healthy cells, desired length of treatment protocol, previous reaction to treatment, molecular markers, genetic markers, pathologic specifics and cytologic specifics.

SUB B21

248. A system for predicting the a progression of cancer in individual patients comprising:

a cancer system model;

a plurality of treatment protocols for treating cancer using drugs, including chemotherapy;

a system model modifier, wherein said cancer system model is modified by the system model modifier based on parameters specific to the individual; and

a predictor to predict the progression of cancer under the plurality of treatment protocols based on the modified system model.

249. The system of claim 248 wherein the system model further comprises:

a realistic process model of cancer development; and

a realistic treatment model that models the effects of treating cancer with drugs, including chemotherapy.

250. The system of claim 249 wherein said process model incorporates a distribution of cycling cells and quiescent cells.

SUB B22

251. The system of claim 249 where a tumor cell cycle is divided into at least four compartments G1, S, G2 and M and a quiescent stage is denoted by G0, wherein each of said four compartments is further subdivided into sub-compartments and an ith sub-compartment representing cells of age in the corresponding compartment, wherein cells entering a compartment always enter a first sub-compartment of the compartment.

252. The system of claim 251 wherein the model traces development of cancer cells using a predetermined set of parameters by calculating a number of cells in each subcompartment using stepwise equations.

253. The system of claim 252 wherein a probability vector is used to determine a fraction of cells that leaves any subcompartment in a compartment to move to a first subcompartment of the next compartment.

254. The system of claim 252 where a set control functions uniquely determine an outcome of every single step, wherein said control functions depend on age of cells, state of a current population and associated environment.

255. The system of claim 252 wherein a tumor is modelled as a combination of a plurality of homogeneous group of cells, each of said homogeneous group of cells representing a

similarly behaving group of cells distributed between all the cell-cycle compartments.

256. The system of claim 255, wherein in each step, a number of cells in each sub-compartment of each compartment of each group is calculated according to factors including a previous state, parameters of tumor, tumor current microenvironment and drug concentration.

257. The system of claim 256 where spatial structure of the tumor is included in the model.

SUB B23

258. The system of claim 257, wherein PK and PD, cytotoxic effects and cytostatic effects of anticancer drugs are incorporated into the model.

259. The system of claim 258 wherein a dose-limiting toxicity is incorporated into the model.

260. The system of claim 248 wherein, said parameters specific to the individual comprise parameters related to tumor dynamics, patient specific drug PK, and dynamics of dose-limiting host tissues.

261. The system of claim 260, wherein said parameters related to tumor dynamics comprise age, weight, gender, percentage of limiting healthy cells, desired length of treatment protocol, previous reaction to treatment, molecular markers, genetic markers, pathologic specifics and cytologic specifics.

SUB B24

262. A system for predicting the a progression of cancer in a general patients comprising:

a cancer system model;

a plurality of treatment protocols for treating cancer using drugs, including chemotherapy; and

a predictor to predict the progression of cancer under the plurality of treatment protocols based on the modified system model.

263. The system of claim 262 wherein the system model further comprises:

a realistic process model of cancer development; and

a realistic treatment model that models the effects of treating cancer with drugs, including chemotherapy.

264. The system of claim 263 wherein said process model incorporates a distribution of cycling cells and quiescent cells.

SUB B25

265. The system of claim 263 where a tumor cell cycle is divided into at least four compartments G1, S, G2 and M and a quiescent stage is denoted by G0, wherein each of said four compartments is further subdivided into sub-compartments and an ith sub-compartment representing cells of age I in the corresponding compartment, wherein cells entering a compartment always enter a first sub-compartment of the compartment.

266. The system of claim 265 wherein the model traces development of cancer cells using a predetermined set of parameters by calculating a number of cells in each subcompartment using stepwise equations.

267. The system of claim 266 wherein a probability vector is used to determine a fraction of cells that leaves any subcompartment in a compartment to move to a first subcompartment of the next compartment.

268. The system of claim 266 where a set control functions uniquely determine an outcome of every single step, wherein said control functions depend on age of cells, state of a current population and associated environment.

269. The system of claim 266 wherein a tumor is modelled as a combination of a plurality of homogeneous group of cells, each of said homogeneous group of cells representing a similarly behaving group of cells distributed between all the cell-cycle compartments.

270. The system of claim 269, wherein in each step, a number of cells in each sub-compartment of each compartment of each group is calculated according to factors including a previous state, parameters of tumor, tumor current microenvironment and drug concentration.

271. The system of claim 270 where spatial structure of the tumor is included in the model.

SUB B26

272. The system of claim 271, wherein PK and PD, cytotoxic effects and cytostatic effects of anticancer drugs are incorporated into the model.

273. The system of claim 272 wherein a dose-limiting toxicity is incorporated into the model.

274. A method of recommending an optimal treatment protocol for an individual comprising:

creating a system model;

enumerating a plurality of treatment protocols;

modifying the system model based on parameters specific to the individual; and

selecting an optimal treatment protocol from said plurality of treatment protocols based on the modified system model.

275. The method of claim 274 wherein the step of creating the system model further comprises:

modelling a biological process; and

realistically modelling effects of a treatment on said biological process.

276. The method of claim 275, wherein said modelling of biological processes is done by mathematical modelling biological processes affecting healthy cell populationss and mathematically modelling biological processes affecting cell populationss with at least one disease.

277. The method of claim 276 wherein said healthy cell populationss include bone-marrow cells and host tissue cells that are affected by said treatment model.

278. The method of claim 276 wherein said cell populationss with at least one disease is one of cancer cells, and diseased bone-marrow cells including diseased Neutrophil cells and diseased Thrompocyte cells.

279. The method of claim 275, wherein said treatment models comprise treatment specific processes that affect cell populationss.

280. The method of claim 279 wherein said treatment specific process is interactions involving at least one of a group comprising pharmacokinetic (PK), pharmacodynamic (PD), cytostatic, cytotoxic, and methods of affecting cell biology and causing cell death, with associated biological processes.

281. The method of claim 274 wherein, said parameters specific to the individual include one or more selected from a group consisting of parameters related to the biological process' dynamics, patient specific drug PK, PD and dynamics of dose-limiting host tissues.

282. The method of claim 281, wherein said parameters related to biological process' dynamics comprise age, weight, gender, blood picture, desired length of treatment protocol, previous reaction to treatment, molecular markers, genetic markers, pathologic specifics and

cytologic specifics.

283. The method of claim 274, wherein user-specific parameters are used in selecting the optimal treatment.

284. The method of claim 283 wherein a fitness function is used to perform the selection.

SUB B27

285. The method of claim 284 wherein said fitness function incorporates at least one parameter selected from a group consisting patient survival, time to death, time to reach a specified disease stage (including cure), tumor load, pathogen load, cytotoxicity, side effects, quality of life, cost of treatment and pain.

286. The method of claim 285, wherein a user can input specific coefficients for said at least one parameter to adjust the fitness function to satisfy the user's goals.

287. The method of claim 283, wherein the user-specific parameters are based on a user, said user being a medical doctor.

288. The method of claim 283, wherein the user-specific parameters are based on a user, said user being a scientist.

289. The method of claim 283, wherein the user-specific parameters are based on a

user, said user being a drug developer.

SUB B28

290. The method of claim 274 wherein said selection of treatment protocols incorporate cytotoxic effects.

291. The method of claim 274 wherein said selection of treatment protocols incorporate drug.

292. The method of claim 274, wherein operation research techniques are used in performing the selection.

293. The method of claim 274, wherein heuristics are used to perform searching and selection.

294. The method of claim 293 wherein, said heuristics comprise computational feasibility.

SUB B29

295. The method of claim 274 wherein said recommendation is a combination of disease and treatment strategy, including types of treatment, , e.g., chemotherapy, radiotherapy, surgery, immunotherapy, etc, device, drug or drug combination, and treatment schedule.

296. A Method of recommending an optimal treatment protocol for a general patient comprising:

creating a system model;

enumerating a plurality of treatment protocols; and

selecting an optimal treatment protocol from said plurality of treatment protocols based on the modified system model.

297. The method of claim 296 wherein the step of creating the system model further comprises:

modelling a biological process; and

realistically modelling effects of a treatment on said biological process.

298. The method of claim 297, wherein said modelling of biological processes is done by mathematical modelling biological processes affecting healthy cell populationss and mathematically modelling biological processes affecting cell populationss with at least one disease.

299. The method of claim 298 wherein said healthy cell populationss include bone-marrow cells and host tissue cells that are affected by said treatment model.

300. The method of claim 298 wherein said cell populationss with at least one disease is one of cancer cells, and diseased bone-marrow cells including diseased Neutrophil cells and diseased Thrompocyte cells.

301. The method of claim 297, wherein said treatment models comprise treatment specific processes that affect cell populationss.

302. The method of claim 301 wherein said treatment specific process is interactions involving one of a group comprising pharmacokinetic, pharmacodynamic, cytostatic, cytotoxic, or any other method of affecting cell biology and causing cell death, with associated biological processes.

303. The method of claim 296, wherein user-specific parameters are used in selecting the optimal treatment.

304. The method of claim 303 wherein a fitness function is used to perform the selection.

SUB B3

305. The method of claim 304 wherein said fitness function incorporates at least one parameter selected from a group comprising patient survival, time to death, time to reach a specified disease stage (including cure), tumor load, pathogen load, cytotoxicity, side effects, quality of life, cost of treatment and pain.

306. The method of claim 305, wherein a user can input specific coefficients for said at least one parameter to adjust the fitness function to satisfy the user's goals.

307. The method of claim 303, wherein the user-specific parameters are based on a user, said user being a medical doctor.

308. The method of claim 303, wherein the user-specific parameters are based on a user, said user being a scientist.

309. The method of claim 303, wherein the user-specific parameters are based on a user, said user being a drug developer.

310. The method of claim 296 wherein said selection of treatment protocols incorporate cytotoxic effects.

311. The method of claim 296 wherein said selection of treatment protocols incorporate drug efficacy.

312. The method of claim 296, wherein operation research techniques are used in performing the selection.

313. The method of claim 296, wherein heuristics are used to perform searching and selection.

314. The method of claim 313 wherein, said heuristics comprise computational feasibility.

315. The method of claim 296 wherein said recommendation is a combination of disease and treatment strategy, including types of treatment, , e.g., chemotherapy, radiotherapy, surgery, immunotherapy, etc, device, drug or drug combination, and treatment schedule.

316. A method of predicting progression of a biological process in an individual patient under a plurality of treatment protocols, wherein said biological process could be related to healthy or diseased processes, said plurality of protocols including no treatment, said method comprising:

creating a system model;

enumerating a plurality of treatment protocols; and

modifying the system model based on parameters specific to the individual.

selecting an optimal treatment protocol from said plurality of treatment protocols based on the modified system model.

317. The method of claim 316 wherein the step of creating a system model further comprises:

realistically modelling a biological process; and

realistically modelling the effects of the treatment on said biological process.

318. The method of claim 317, wherein said step of modelling a biological process comprises creating a mathematical model for biological processes affecting healthy cell populations and creating a biological processes affecting cell populations with at least one disease.

319. The method of claim 318 wherein said healthy cell populations include bone-marrow cells and host tissue cells that are affected by said treatment model.

Sub B34

320. The method of claim 318 wherein said cell populationss with at least one disease is one of cancer cells, and diseased bone-marrow cells including diseased Neutrophil cells and diseased Thrombocyte cells.

321. The method of claim 317, wherein said treatment models comprise treatment specific processes that affect cell populationss.

322. The method of claim 321 wherein said treatment specific process is interactions involving one of a group comprising PK, PD, drug cytostatics, drug cytotoxics, or any other method of affecting cell biology and causing cell death, with associated biological processes.

323. The method of claim 316 wherein, said parameters specific to the individual include one or more selected from a group consisting of parameters related to the biological process' dynamics, patient specific drug PK, PD and dynamics of dose-limiting host tissues.

324. The method of claim 323, wherein said parameters related to biological process' dynamics comprise age, weight, gender, blood picture, desired length of treatment protocol, previous reaction to treatment, molecular markers, genetic markers, pathologic specifics and cytologic specifics.

Sub B35

325. A method of predicting progression of a biological process in a general patient under a plurality of treatment protocols, wherein said biological process could be related to

healthy or diseased, said plurality of protocols including no treatment, said method comprising:

creating a system model;

enumerating a plurality of treatment protocols; and

selecting an optimal treatment protocol from said plurality of treatment protocols based on the modified system model.

326. The method of claim 325 wherein the step of creating a system model further comprises:

realistically modelling a biological process; and

realistically modelling the and the effects of the treatment on said biological process.

327. The method of claim 326, wherein said step of modelling a biological process comprises creating a mathematical model for biological processes affecting healthy cell populations and creating a biological processes affecting cell populations with at least one disease.

328. The method of claim 327 wherein said healthy cell populations include bone-marrow cells and host tissue cells that are affected by said treatment model.

SUB B36

329. The method of claim 327 wherein said cell populations with at least one disease is one of cancer cells, and diseased bone-marrow cells including at least one of diseased Neutrophil cells and diseased Thrombocyte cells.

330. The method of claim 326, wherein said treatment models comprise treatment specific processes that affect cell populations.

SUB B37

331. The method of claim 330 wherein said treatment specific process is interactions involving one of a group comprising PK, PD cytostatic, cytotoxic, and methods of affecting cell biology and causing cell death, with associated biological processes.

332. A method for modelling Thrombopietic lineage in an individual, said method comprising:

realistically modelling a process to create a process model for cells involved in Thrombopoiesis; and

modifying the process model based on parameters specific to the individual.

333. The method of claim 332 wherein a realistic progression of cells involved indiseased Thrombopoiesis is incorporated in the process model.

334. The method of claim 333 wherein diseased Thrombopoiesis includes Thrombocytopenia.

335. The method of claim 333 wherein effects of at least one drug in the realistic progression of cells involved in Thrombopoiesis is incorporated.

336. The method of claim 335 wherein said at least one drug is Thrombopoietin (TPO).

337. The method of claim 333 wherein said process model imitates a course of the individual's bone marrow progression, peripheral platelet counts and TPO concentration changes.

338. The method of claim 333, wherein said process model incorporates cell-suppressive treatment effects and administration of TPO to the patient.

339. The method of claim 338, wherein said cell-suppressive treatment is chemotherapy.

340. The method of claim 333, wherein said method is used for recommending an optimum treatment protocol, and wherein said method further comprises:

enumerating a plurality of treatment protocols; and

selecting an optimal treatment protocol from said plurality of treatment protocols based on the modified system model.

341. A method for modelling Thrombopietic lineage in a general patient, said method comprising:

realistically modelling a process to create a process model for cells involved in Thrombopoiesis.

342. The method of claim 341 wherein a realistic progression of cells involved

indiseased throbmopoiesis is incorporated in the process model.

343. The method of claim 342 wherein diseased Thrombopoiesis includes Thrombocytopenia.

344. The method of claim 342 wherein effects of at least one drug in the realistic progression of cells involved in Thrombopoiesis is incorporated.

345. The method of claim 344 wherein said at least one drug is Thrombopoietin (TPO).

346. The method of claim 342 wherein said process model imitates a course of the individual's bone marrow progression, peripheral platelet counts and TPO concentration changes.

347. The method of claim 342, wherein said process model incorporates cell-suppressive treatment effects and administration of TPO to the patient.

348. The method of claim 347, wherein said cell-suppressive treatment is chemotherapy.

349. The method of claim 342, wherein said method is used for recommending an optimum treatment protocol, and wherein said method further comprises:

enumerating a plurality of treatment protocols; and

selecting an optimal treatment protocol from said plurality of treatment protocols based on the modified system model.

350. A method for predicting progression of Thrombopoiesis and Thrombocytopenia for an individual under a plurality of treatment protocols, said plurality of protocols including no treatment, said method comprising:

creating a realistic model of Thrombopoiesis and Thrombocytopenia;

generating a plurality of treatment protocols for affecting Thrombopoiesis and treatingThrombocytopenia using at least one drug;

modifying the model based on parameters specific to the individual; and

predicting the progression of the disease or the natural biological process under said plurality of treatment protocols based on the modified system model.

351. The method of claim 350 wherein the model incorporates a realistic progression of cells involved indiseased Thrombopoiesis.

352. The method of claim 351 wherein diseased Thrombopoiesis includes Thrombocytopenia.

353. The method of claim 351 wherein the model incorporates effects of at least one drug in the realistic progression of cells involved in Thrombocytopenia.

354. The method of claim 353 wherein said at least one drug is Thrombopoietin (TPO).

355. The method of claim 351 wherein the model imitates a course of the individual's bone marrow progression, peripheral platelet counts and TPO concentration changes.

356. The method of claim 351, wherein the model incorporates cell-suppressive treatment effects and administration of TPO to the patient.

357. The method of claim 356, wherein said cell-suppressive treatment is chemotherapy.

358. The method of claim 351 wherein said process model further comprises a plurality of compartments.

359. The method of claim 358 wherein said compartments include:

a stem cell (SC) compartment that comprises bone marrow hemopoietic progenitors that have an ability to differentiate into more than one cell line wherein cells in the stem cell compartment proliferate and differentiate into one of megakaryocyte progenitors;

a colony forming units - megakaryocytes (CFU-Meg) compartment, wherein the megakaryocyte progenitors get committed as a megakaryocyte line and spend some time multiplying and maturing;

a megakaryoblast (MKB) compartment, which receives the cells from CFU-Meg, wherein the cells in the MKB compartment have lost their ability to proliferate but are not mature to release platelets;

a MK16 compartment, which receives cells from the MKB compartment, wherein a subset of cells in the MK16 compartment release platelets at a constant rate until they exhaust their capacity and are disintegrated and a second subset of cells do not release platelets but continue with endomitosis;

a MK32 compartment that receives cells from the MK16 compartment, wherein a subset of cells in this compartment release platelets and a second subset of cells do not release platelets but continue with endomitosis;

a MK64 compartment that receives cells from the MK32 compartment wherein a subset of cells in this compartment release platelets and a second subset of cells do not release platelets but continue with endomitosis;

a MK128 compartment that receives cells from the MK64 compartment wherein a subset of cells in this compartment release platelets;

a platelets (PL) compartment.

360. The method of claim 359 wherein an effect of apoptosis are included with an overall effect of cell proliferation in giving rise to an amplification of cell numbers in a corresponding compartment.

361. The method of claim 359 wherein the model further incorporates the effects of TPO on the SC, CFU-Meg and MKB compartments.

362. The method of claim 361 wherein the effects are expressed in terms of effects of TPO concentration on amplification rate, rate of cell maturation and a fraction of cells that

undergo endomotisis.

363. The method of claim 362 wherein when the TPO concentration is above a predetermined threshold level, the amplification rate of cells in the SC compartment are affected and below the threshold the amplification rate is dependent only on a current number of cells.

364. The method of claim 361 wherein in the CFU-Meg compartment the cells are sensitive to TPO concentration regardless of the concentration of TPO.

365. The method of claim 361, wherein the transit time is same in all platelet releasing compartments and the transit time of the SC, CFU-Meg and MKB compartments are functions of micro-environmental conditions.

366. The method of claim 365 wherein in the SC compartment when the TPO concentration is above the threshold, the transit time is shortened based the dose.

367. The method of claim 365 wherein in the CFU-Meg and MKB, the transit time is solely based on TPO concentration.

368. The method of claim 361 wherein a fraction of cells in the SC compartment that commits to megakaryocytic lineage is constant.

369. The method of claim 361 wherein in the CFU-Meg and MKB compartments,

every mature cell passes on to the next compartment.

370. The method of claim 361 wherein in the MK16, MK32 and MK64 compartments, a fraction of cells pass on to the next compartment, said fraction being dependent on the TPO concentration.

371. The method of claim 361 wherein cells from MK128 compartment do not flow into any other compartment.

372. The method of claim 358, wherein each of said compartments is further divided into sub-compartments, each of said sub-compartments containing cells of a specific age in hours.

373. The method of claim 372 wherein cells that spend all their corresponding transit time in a given compartment pass on to the next compartment, wherein cells that have left a corresponding compartment each hour fill the first sub-compartment of the next compartment.

374. The method of claim 373, wherein the platelet releasing cells contribute platelets to the first sub-compartment of the PL compartment.

375. A method for predicting progression of Thrombopoiesis and Thrombocytopenia for a general patient under a plurality of treatment protocols, said plurality of protocols including no treatment, said method comprising:

creating a realistic model Thrombopoiesis andThrombocytopenia;

generating a plurality of treatment protocols for affecting Thrombopoiesis and treatingThrombocytopenia using at least one drug; and

predicting the progression of the disease or the natural biological process under said plurality of treatment protocols based on the modified system model.

376. The method of claim 375 wherein the model incorporates a realistic progression of cells involved indiseased Thrombopoiesis.

377. The method of claim 376 wherein diseased Thrombopoiesis includes Thrombocytopenia.

378. The method of claim 376 wherein the model incorporates effects of at least one drug in the realistic progression of cells involved in Thrombocytopenia.

379. The method of claim 378 wherein said at least one drug is Thrombopoietin (TPO).

380. The method of claim 376 wherein the model imitates a course of the individual's bone marrow progression, peripheral platelet counts and TPO concentration changes.

381. The method of claim 376, wherein the model incorporates cell-suppressive treatment effects and administration of TPO to the patient.

382. The method of claim 381, wherein said cell-suppressive treatment is chemotherapy.

383. The method of claim 376 wherein said process model further comprises a plurality of compartments.

384. The method of claim 383 wherein said compartments include:

a stem cell (SC) compartment that comprises bone marrow hemopoietic progenitors that have an ability to differentiate into more than one cell line wherein cells in the stem cell compartment proliferate and differentiate into one of megakaryocyte progenitors;

a colony forming units - megakaryocytes (CFU-Meg) compartment, wherein the megakaryocyte progenitors get committed as a megakaryocyte line and spend some time multiplying and maturing;

a megakaryoblast (MKB) compartment, which receives the cells from CFU-Meg, wherein the cells in the MKB compartment have lost their ability to proliferate but are not mature to release platelets;

a MK16 compartment, which receives cells from the MKB compartment, wherein a subset of cells in the MK16 compartment release platelets at a constant rate until they exhaust their capacity and are disintegrated and a second subset of cells do not release platelets but continue with endomitosis;

a MK32 compartment that receives cells from the MK16 compartment, wherein a subset of cells in this compartment release platelets and a second subset of cells do not release platelets but continue with endomitosis;

a MK64 compartment that receives cells from the MK32 compartment wherein a subset of cells in this compartment release platelets and a second subset of cells do not release platelets but continue with endomitosis;

a MK128 compartment that receives cells from the MK64 compartment wherein a subset of cells in this compartment release platelets;

a platelets (PL) compartment.

385. The method of claim 384 wherein an effect of apoptosis are included with an overall effect of cell proliferation in giving rise to an amplification of cell numbers in a corresponding compartment.

386. The method of claim 384 wherein the model further incorporates the effects of TPO on the SC, CFU-Meg and MKB compartments.

387. The method of claim 386 wherein the effects are expressed in terms of effects of TPO concentration on amplification rate, rate of cell maturation and a fraction of cells that undergo endomotisis.

388. The method of claim 387 wherein when the TPO concentration is above a predetermined threshold level, the amplification rate of cells in the SC compartment are affected and below the threshold the amplification rate is dependent only on a current number of cells.

389. The method of claim 386 wherein in the CFU-Meg compartment the cells are

sensitive to TPO concentration regardless of the concentration of TPO.

390. The method of claim 386, wherein the transit time is same in all platelet releasing compartments and the transit time of the SC, CFU-Meg and MKB compartments are functions of micro-environmental conditions.

391. The method of claim 390 wherein in the SC compartment when the TPO concentration is above the threshold, the transit time is shortened based the dose.

392. The method of claim 390 wherein in the CFU-Meg and MKB, the transit time is solely based on TPO concentration.

393. The method of claim 386 wherein a fraction of cells in the SC compartment that commits to megakaryocytic lineage is constant.

394. The method of claim 386 wherein in the CFU-Meg and MKB compartments, every mature cell passes on to the next compartment.

395. The method of claim 386 wherein in the MK16, MK32 and MK64 compartments, a fraction of cells pass on to the next compartment, said fraction being dependent on the TPO concentration.

396. The method of claim 386 wherein cells from MK128 compartment do not flow

into any other compartment.

397. The method of claim 383, wherein each of said compartments is further divided into sub-compartments, each of said sub-compartments containing cells of a specific age in hours.

398. The method of claim 397 wherein cells that spend all their corresponding transit time in a given compartment pass on to the next compartment, wherein cells that have left a corresponding compartment each hour fill the first sub-compartment of the next compartment.

399. The method of claim 398, wherein the platelet releasing cells contribute platelets to the first sub-compartment of the PL compartment.

400. A method for modelling Neutrophil lineage for an individual, said method comprising:

creating a realistic a Neutrophil system model including a realistic process model for cells involved in Neutrophil lineage; and

5 modifying the system model based on parameters specific to the individual.

401. The method of claim 400 wherein the system model incorporates a realistic progression of cells involved in Granulopoietic disorders, including Neutropenia.

402. The method of claim 401 wherein the system model incorporates effects of at

least one drug in the realistic progression of cells involved in Granulopoiesis and Neutropenia.

403. The method of claim 402 wherein said at least one drug is Granulocyte Colony Stimulating Factor (G-CSF).

404. The method of claim 403 wherein said system model comprises at least three stages,

a first stage related to an administered amount of cytokine;

a second stage representing a pharmacokinetic behavior of G-CSF; and

a third stage representing a phrmacodynamic effect of G-CSF on kinetic parameters of the system.

405. The method of claim 400 wherein said model comprises a mitotic compartment, and a post mitotic compartment, said mitotic compartment being divided into subcompartments wherein a kth sub-compartment contains cells of age between k-1 and k hours relative to a time of entry into the mitotic compartment.

406. The method of claim 405, wherein effects of toxic drugs, including chemotherapy are incorporated by mapping various cell-cycle phases to the sub-compartments and formulating a function of cytotoxic effects of toxic drugs, including chemotherapy on the cell-cycle phases.

407. The method of claim 405 wherein the effects of G-CSF on the mitotic compartment are modeled as an increase in a rate of cells entering the myeloblasts compartment

from an uncommitted stem cell pool.

408. The method of claim 405 wherein the post-mitotic compartment is modeled as a single pool of cells wherein cells in a last sub-compartment of the mitotic compartment enters the post-mitotic compartment and a proportion of cells within the post-mitotic compartment enters a Neutrophil pool every hour.

409. The method of claim 405 wherein effects of G-CSF on the Neutrophil lineage are modeled as a decrease in the cells in the post-mitotic compartment which is subsequently compensated by an increased production in the mitotic compartment, said compensation sustaining an increase in mature Neutrophil count.

410. The method of claim 405, wherein an elimination of Neutrophils in the post-mitotic compartment is represented by a Poisson distribution.

411. The method of claim 405, wherein the cytotoxic effects of toxic drugs, including chemotherapy in the post-mitotic compartment is modeled as an effect on a single pool of cells.

412. The method of claim 405, wherein kinetic of G-CSF is modeled as an exponential distribution.

413. The method of claim 401, wherein a selection of an optimal treatment uses an objective function that aims at minimizing G-CSF administration and returning Neutrophil

lineage to normal levels.

414. The method of claim 413, wherein said selection is performed using linear programming.

415. The method of claim 414, wherein phrmacokinetics and pharmacodynamics of G-CSF are defined using piecewise linear functions.

416. The method of claim 400, wherein said method is used for recommending an optimum treatment protocol, and wherein said method further comprises:

enumerating a plurality of treatment protocols; and

selecting an optimal treatment protocol from said plurality of treatment protocols based on the modified system model.

417. A method for modelling Neutrophil lineage for a general patient, said method comprising:

creating a realistic a Granulopoiesis system model including a realistic process model for cells involved in Granulopoiesis lineage.

418. The method of claim 417 wherein the system model incorporates a realistic progression of cells involved in Granulopoietic disorders, including Neutropenia.

419. The method of claim 418 wherein the system model incorporates effects of at

least one drug in the realistic progression of cells involved Granulopoiesis and in Neutropenia.

420. The method of claim 419 wherein said at least one drug is Granulocyte Colony Stimulating Factor (G-CSF).

421. The method of claim 420 wherein said system model comprises at least three stages,

a first stage related to an administered amount of cytokine;

a second stage representing a pharmacokinetic behavior of G-CSF; and

a third stage representing a phrmacodynamic effect of G-CSF on kinetic parameters.

422. The method of claim 417 wherein said model comprises a mitotic compartment, and a post mitotic compartment, said mitotic compartment being divided into subcompartments wherein a kth sub-compartment contains cells of age between k-1 and k hours relative to a time of entry into the mitotic compartment.

423. The method of claim 422, wherein effects of toxic drugs, including chemotherapy are incorporated by mapping various cell-cycle phases to the sub-compartments and formulating a function of cytotoxic effects of toxic drugs, including chemotherapy on the cell-cycle phases.

424. The method of claim 422 wherein the effects of G-CSF on the mitotic compartment are modeled as an increase in a rate of cells entering the myeloblasts compartment from an uncommitted stem cell pool.

425. The method of claim 422 wherein the post-mitotic compartment is modeled as a single pool of cells wherein cells in a last sub-compartment of the mitotic compartment enters the post-mitotic compartment and a proportion of cells within the post-mitotic compartment enters a Neutrophil pool every hour.

426. The method of claim 422 wherein effects of G-CSF on the Neutrophil lineage are modeled as a decrease in the cells in the post-mitotic compartment which is subsequently compensated by an increased production in the mitotic compartment, said compensation sustaining an increase in mature Neutrophil count.

427. The method of claim 422, wherein an elimination of Neutrophils in the post-mitotic compartment is represented by a Poisson distribution.

428. The method of claim 422, wherein the cytotoxic effects of toxic drugs, including chemotherapy in the post-mitotic compartment is modeled as an effect on a single pool of cells.

429. The method of claim 422 wherein kinetic of G-CSF is modeled as an exponential distribution.

430. The method of claim 418, wherein a selection of an optimal treatment uses an objective function that aims at minimizing G-CSF administration and returning Neutrophil lineage to normal levels.

431. The method of claim 430, wherein said selection is performed using linear programming.

432. The method of claim 431, wherein phrmacokinetics and pharmacodynamics of G-CSF are defined using piecewise linear functions.

433. The method of claim 417 wherein said method is used for recommending an optimum treatment protocol, and wherein said method further comprises:

enumerating a plurality of treatment protocols; and

selecting an optimal treatment protocol from said plurality of treatment protocols based on the modified system model.

434. A method for predicting progression of Granulopoiesis for an individual under a plurality of treatment protocols, said plurality of protocols including no treatment, said system comprising:

creating a Neutrophil system model including a realistic process model for cells involved in Neutrophil production;

generating a plurality of treatment protocols; and

modifying the system model modifier, wherein said Neutrophil system model is modified by the system model modifier based on parameters specific to the individual; and

predicting the progression under the plurality of treatment protocols based on the modified system model.

435. The method of claim 434 wherein the system model incorporates a realistic progression of cells involved in Granulopoietic disorders, including Neutropenia.

436. The method of claim 435 wherein the system incorporates effects of at least one drug in the realistic progression of cells involved in Granulopoiesis and Neutropenia.

437. The system of claim 436 wherein said at least one drug is Granulocyte Colony Stimulating Factor (G-CSF).

438. The method of claim 437 wherein said model comprises at least three stages,

a first stage related to an administered amount of cytokine;

a second stage representing a pharmacokinetic behavior of G-CSF; and

a third stage representing a phrmacodynamic effect of G-CSF on kinetic parameters.

439. The method of claim 434 wherein said model comprises a mitotic compartment, and a post mitotic compartment, said mitotic compartment being divided into subcompartments wherein a kth sub-compartment contains cells of age between k-1 and k hours relative to a time of entry into the mitotic compartment.

440. The method of claim 439, wherein effects of toxic drugs, including chemotherapy are incorporated by mapping various cell-cycle phases to the sub-compartments and formulating a function of cytotoxic effects of toxic drugs, including chemotherapy on the cell-cycle phases.

441. The method of claim 439 wherein the effects of G-CSF on the mitotic compartment are modeled as an increase in a rate of cells entering the myeloblasts compartment from an uncommitted stem cell pool.

442. The method of claim 439 wherein the post-mitotic compartment is modeled as a single pool of cells wherein cells in a last sub-compartment of the mitotic compartment enters the post-mitotic compartment and a proportion of cells within the post-mitotic compartment enters a Neutrophil pool every hour.

443. The method of claim 439 wherein effects of G-CSF on the Neutrophil lineage are modeled as a decrease in the cells in the post-mitotic compartment which is subsequently compensated by an increased production in the mitotic compartment, said compensation sustaining an increase in mature Neutrophil count.

444. The method of claim 439, wherein an elimination of Neutrophils in the post-mitotic compartment is represented by a Poisson distribution.

445. The method of claim 439, wherein the cytotoxic effects of toxic drugs, including chemotherapy in the post-mitotic compartment is modeled as an effect on a single pool of cells.

446. The method of claim 439, wherein kinetic of G-CSF is modeled as an exponential distribution.

447. The method of claim 435, wherein a selection of an optimal treatment uses an objective function that aims at minimizing G-CSF administration and returning Neutrophil lineage to normal levels.

448. The method of claim 447, wherein said selection is performed using linear programming.

449. The method of claim 448, wherein phrmacokinetics and pharmacodynamics of G-CSF are defined using piecewise linear functions.

450. A method for predicting progression of Granulopoiesis for a general patient under a plurality of treatment protocols, said plurality of protocols including no treatment, said system comprising:

creating a Neutrophil system model including a realistic process model for cells involved in Neutrophil production;

generating a plurality of treatment protocols; and

predicting the progression under the plurality of treatment protocols based on the modified system model.

451. The method of claim 450 wherein the system model incorporates a realistic progression of cells involved in Granulopoietic disorders, including Neutropenia.

452. The method of claim 451 wherein the system incorporates effects of at least one drug in the realistic progression of cells involved in Granulopoiesis and Neutropenia.

453. The system of claim 452 wherein said at least one drug is Granulocyte Colony Stimulating Factor (G-CSF).

454. The method of claim 453 wherein said model comprises at least three stages,

a first stage related to an administered amount of cytokine;

a second stage representing a pharmacokinetic behavior of G-CSF; and

a third stage representing a phrmacodynamic effect of G-CSF on kinetic parameters.

455. The method of claim 450 wherein said model comprises a mitotic compartment, and a post mitotic compartment, said mitotic compartment being divided into subcompartments wherein a kth sub-compartment contains cells of age between k-1 and k hours relative to a time of entry into the mitotic compartment.

456. The method of claim 455, wherein effects of toxic drugs, including chemotherapy are incorporated by mapping various cell-cycle phases to the sub-compartments and formulating a function of cytotoxic effects of toxic drugs, including chemotherapy on the cell-cycle phases.

457. The method of claim 455 wherein the effects of G-CSF on the mitotic compartment are modeled as an increase in a rate of cells entering the myeloblasts compartment from an uncommitted stem cell pool.

458. The method of claim 455 wherein the post-mitotic compartment is modeled as a single pool of cells wherein cells in a last sub-compartment of the mitotic compartment enters the post-mitotic compartment and a proportion of cells within the post-mitotic compartment enters a Neutrophil pool every hour.

459. The method of claim 455 wherein effects of G-CSF on the Neutrophil lineage are modeled as a decrease in the cells in the post-mitotic compartment which is subsequently compensated by an increased production in the mitotic compartment, said compensation sustaining an increase in mature Neutrophil count.

460. The method of claim 455, wherein an elimination of Neutrophils in the post-mitotic compartment is represented by a Poisson distribution.

461. The method of claim 455, wherein the cytotoxic effects of toxic drugs, including chemotherapy in the post-mitotic compartment is modeled as an effect on a single pool of cells.

462. The method of claim 455, wherein kinetic of G-CSF is modeled as an exponential distribution.

463. The method of claim 451, wherein a selection of an optimal treatment uses an objective function that aims at minimizing G-CSF administration and returning Neutrophil lineage to normal levels.

464. The method of claim 463, wherein said selection is performed using linear programming.

465. The method of claim 464, wherein phrmacokinetics and pharmacodynamics of G-CSF are defined using piecewise linear functions.

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466. A method for recommending an optimal treatment protocol for treating cancer using drugs , including chemotherapy, for an individual, said method comprising:

creating a cancer system model;

enumerating a plurality of treatment protocols for treating cancer using drugs, including chemotherapy;

modifying the system model based on parameters specific to the individual; and

selecting an optimal treatment protocol from said plurality of treatment protocols based on the modified system model.

467. The method of claim 466 wherein the system model further comprises:

a realistic process model of cancer development; and

a realistic treatment model that models the effects of treating cancer with drugs, including chemotherapy.

468. The method of claim 467 wherein said process model incorporates a distribution of cycling cells and quiescent cells.

469. The method of claim 467 where a tumor cell cycle is divided into at least four compartments G1, S, G2 and M and a quiescent stage is denoted by G0, wherein each of said four compartments is further subdivided into sub-compartments and an ith sub-compartment representing cells of age I in the corresponding compartment, wherein cells entering a compartment always enter a first sub-compartment of the compartment.

470. The method of claim 469 wherein the model traces development of cancer cells using a predetermined set of parameters by calculating a number of cells in each subcompartment using stepwise equations.

471. The method of claim 470 wherein a probability vector is used to determine a fraction of cells that leaves any subcompartment in a compartment to move to a first subcompartment of the next compartment.

472. The method of claim 470 where a set control functions uniquely determine an outcome of every single step, wherein said control functions depend on age of cells, state of a current population and associated environment.

473. The method of claim 470 wherein a tumor is modelled as a combination of a plurality of homogeneous group of cells, each of said homogeneous group of cells representing a similarly behaving group of cells distributed between all the cell-cycle compartments.

474. The method of claim 473, wherein in each step, a number of cells in each sub-compartment of each compartment of each group is calculated according to factors including a previous state, parameters of tumor, tumor current microenvironment and drug concentration.

475. The method of claim 474 where spatial structure of the tumor is included in the model.

476. The method of claim 475, wherein PK and PD, cytotoxic effects,cytostatic effects and other effects on cell disintegration of anticancer drugs are incorporated into the model.

477. The method of claim 476 wherein a dose-limiting toxicity is incorporated into the model.

478. The method of claim 466 wherein, said parameters specific to the individual comprise parameters related to tumor dynamics, patient specific drug PK, and dynamics of dose-limiting host tissues.

479. The method of claim 478, wherein said parameters related to tumor dynamics comprise age, weight, gender, percentage of limiting healthy cells, desired length of treatment protocol, previous reaction to treatment, molecular markers, genetic markers, pathologic specifics and cytologic specifics.

480. A method of predicting a progression of cancer in an individual, said method

comprising:

creating a cancer system model;

enumerating a plurality of treatment protocols for treating cancer using drugs, including chemotherapy;

modifying the system model based on parameters specific to the individual; and

selecting an optimal treatment protocol from said plurality of treatment protocols based on the modified system model.

481. The method of claim 480 wherein the system model further comprises:

a realistic process model of cancer development; and

a realistic treatment model that models the effects of treating cancer with drugs, including chemotherapy.

482. The method of claim 481 wherein said process model incorporates a distribution of cycling cells and quiescent cells.

483. The method of claim 481 where a tumor cell cycle is divided into at least four compartments G1, S, G2 and M and a quiescent stage is denoted by G0, wherein each of said four compartments is further subdivided into sub-compartments and an ith sub-compartment representing cells of age I in the corresponding compartment, wherein cells entering a compartment always enter a first sub-compartment of the compartment.

484. The method of claim 483 wherein the model traces development of cancer cells

using a predetermined set of parameters by calculating a number of cells in each subcompartment using stepwise equations.

485. The method of claim 484 wherein a probability vector is used to determine a fraction of cells that leaves any subcompartment in a compartment to move to a first subcompartment of the next compartment.

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486. The method of claim 484 where a set control functions uniquely determine an outcome of every single step, wherein said control functions depend on age of cells, state of a current population and associated environment.

487. The method of claim 484 wherein a tumor is modelled as a combination of a plurality of homogeneous group of cells, each of said homogeneous group of cells representing a similarly behaving group of cells distributed between all the cell-cycle compartments.

488. The method of claim 487, wherein in each step, a number of cells in each sub-compartment of each compartment of each group is calculated according to factors including a previous state, parameters of tumor, tumor current microenvironment and drug concentration.

489. The method of claim 488 where spatial structure of the tumor is included in the model.

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490. The method of claim 489, wherein PK and PD, cytotoxic and other cell

disintegration effects , and cytostatic effects of anticancer drugs are incorporated into the model.

491. The method of claim 490 wherein a dose-limiting toxicity is incorporated into the model.

492. The method of claim 480 wherein, said parameters specific to the individual comprise parameters related to tumor dynamics, patient specific drug PK, and dynamics of dose-limiting host tissues.

493. The method of claim 492, wherein said parameters related to tumor dynamics comprise age, weight, gender, percentage of limiting healthy cells, desired length of treatment protocol, previous reaction to treatment, molecular markers, genetic markers, pathologic specifics and cytologic specifics.

494. A method of predicting a progression of cancer in a general patient, said method comprising:

creating a cancer system model;

enumerating a plurality of treatment protocols for treating cancer using drugs, including chemotherapy; and

selecting an optimal treatment protocol from said plurality of treatment protocols based on the modified system model.

495. The method of claim 494 wherein the system model further comprises:

a realistic process model of cancer development; and

a realistic treatment model that models the effects of treating cancer with drugs, including chemotherapy.

496. The method of claim 495 wherein said process model incorporates a distribution of cycling cells and quiescent cells.

497. The method of claim 495 where a tumor cell cycle is divided into at least four compartments G1, S, G2 and M and a quiescent stage is denoted by G0, wherein each of said four compartments is further subdivided into sub-compartments and an ith sub-compartment representing cells of age I in the corresponding compartment, wherein cells entering a compartment always enter a first sub-compartment of the compartment.

498. The method of claim 497 wherein the model traces development of cancer cells using a predetermined set of parameters by calculating a number of cells in each subcompartment using stepwise equations.

499. The method of claim 498 wherein a probability vector is used to determine a fraction of cells that leaves any subcompartment in a compartment to move to a first subcompartment of the next compartment.

500. The method of claim 498 where a set control functions uniquely determine an outcome of every single step, wherein said control functions depend on age of cells, state of a

current population and associated environment.

501. The method of claim 498 wherein a tumor is modelled as a combination of a plurality of homogeneous group of cells, each of said homogeneous group of cells representing a similarly behaving group of cells distributed between all the cell-cycle compartments.

502. The method of claim 501, wherein in each step, a number of cells in each sub-compartment of each compartment of each group is calculated according to factors including a previous state, parameters of tumor, tumor current microenvironment and drug concentration.

503. The method of claim 502 where spatial structure of the tumor is included in the model.

504. The method of claim 503, wherein PK and PD, cytotoxic effects and cytostatic effects of anticancer drugs are incorporated into the model.

505. The method of claim 504 wherein a dose-limiting toxicity is incorporated into the model.

506. A computer program product, including a computer readable medium, said program product comprising a set of instruction to enable a computer system to aid in recommending an optimal treatment protocol for an individual comprising:

a system model code;

treatment protocol code for a plurality of treatment protocols;

a system model modifier code , wherein said system model is modified by the system model modifier based on parameters specific to the individual; and

a selector code to select an optimal treatment protocol from said plurality of treatment protocols based on the modified system model.

507. The computer program product of claim 506 wherein the system model code further comprises:

a realistic biological process model code; and

a realistic treatment model code that enables a computer to model the effects of a treatment on the biological process.

508. A computer program product, including a computer readable medium, said program product comprising a set of instructions to enable a computer system to aid in recommending an optimal treatment protocol for a general patient comprising:

a system model code;

treatment protocol code for a plurality of treatment protocols; and

a selector code to select an optimal treatment protocol from said plurality of treatment protocols based on the modified system model.

509. The computer program product of claim 508 wherein the system model code further comprises:

a realistic biological process model code; and

a realistic treatment model code that enables a computer to model the effects of a

5 treatment on the biological process.